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AN OVERVIEW OF THE DEVELOPMENTS IN PLATELET-RICH PLASMA RESEARCH AND ITS CLINICAL USE

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Abstract

Since its invention in the 1970s, platelet-rich plasma (PRP) has been used in numerous fields, including hair loss, ligament repair, wound healing, and tissue regeneration. We concentrate on PRP administration in musculoskeletal rehabilitation in this review. PRP has a higher platelet concentration than normal since it is an autogenous blood plasma component. An overview of PRP's uses and research findings from randomised controlled trials conducted over the previous five years is what this review article attempts to deliver. In addition to discussing the various PRP classification schemes, the article highlights the significance of comprehending the factors influencing clinical outcomes and highlights the expansion of PRP in the market. Standardized reporting is necessary to ascertain PRP's full potential and the best ways to prepare and administer it, even if studies have shown its clinical utility.

Introduction

Platelet-rich plasma (PRP) is an autologous blood product acquired from part of the plasma fraction created via centrifugation of whole blood. By definition it has a platelet concentration above that of normal physiological levels (1). The term PRP originated in the 1970s by hematologists describing plasma with a platelet count higher than peripheral blood, (2) which at the time was being used as a transfusion product in thrombocytopenic patients. Since then, it has been applied in multiple fields including plastic surgery, pediatric surgery, cardiac surgery, gynecology, urology, and ophthalmology. (3) Platelet-rich plasma (PRP) is a biological product obtained from autologous peripheral blood after centrifugation. These cells harbor three types of granules: dense, α, and lysosomal granules. Closer to the erythrocyte layer, there is typically a high concentration of neutrophils and other granulocytes, alongside a moderate number of platelets. A standardized nomenclature system, such as Dohan Ehrenfest's shorthand naming convention, categories different types of PRP, primarily based on the depth of buffy coat collection.

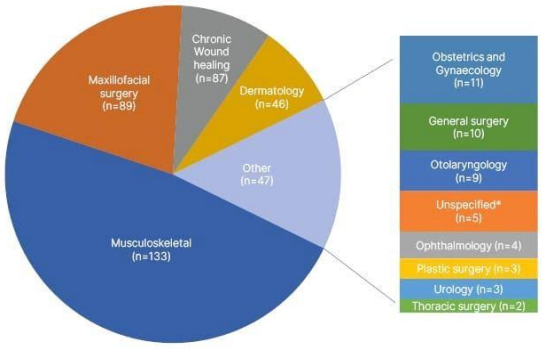

Figure 1: Breakdown of randomised controlled trials on PubMed over the past 5years using platelet-rich plasma (n=402).

While a comprehensive understanding of the crucial elements that drive the benefits of PRP in various fields often remains elusive in literature, attempts are frequently made to conjecture the contributing factors to the benefits observed with PRP use.

Methods:

Search Strategy for PRP. Original English studies published between January 1983 and June 2020 were

searched. The electronic databases used for the search were PubMed, EMBASE, Web of Science, the Cochrane Library, EBSCO (CINAHL), Spine journal, BMC, NCBI, Oxford Academic, Science Direct. There were no language restrictions. We conducted a broad search using the following keywords or text words: "PRP", "History of PRP", "PRP devices", "Molecular mechanism of PRP", "Clinical application of PRP", and "Limitations of PRP". We also searched for the following medical subject headings: "PRP".

1. Selection criteria:

Yielded papers were evaluated independently by two authors and selected if containing pertinence to PRP regarding one or more of the following areas: preparation, classification, mechanism of action, or clinical application within trauma and orthopedics. Papers not written in English and animal studies relating to applications were excluded. The authors acknowledge an element of language bias; however, using more modern publications limits the extent of exclusion.

2. Literature grading and analysis:

Studies were independently rated by two authors using the Oxford Centre for Evidence-based Medicine 'Levels of evidence' document (29) and the Coleman modified score (CMS) when applicable. The review of the literature was conducted following a structured approach to ensure the inclusion of all relevant studies and data regarding the clinical use of PRP across diverse medical fields. Emphasis was laid on the most frequent use cases and documented effectiveness [4]. The search, initiated on 11th January 2023, focused on randomized controlled trials (RCT) from the past 5 years. The electronic database PubMed was utilized, employing the Medical Subject Heading term "Platelet-Rich Plasma" to yield 402 pertinent articles.

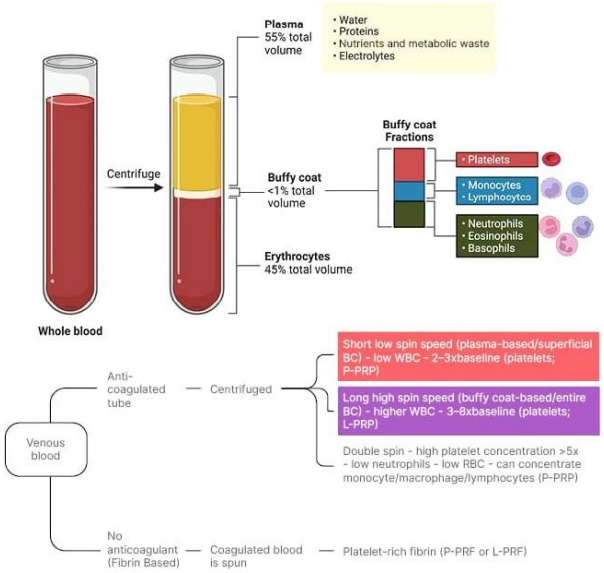

Figure 2: Platelet-rich plasma collection method.

Post-retrieval, abstracts of the identified articles were examined for relevance, followed by a detailed review of the full-text versions. Studies were then stratified into distinct thematic groups based on their outcomes, enabling a comprehensive summary of each field. Further, each study was critically assessed for limitations, contributing to the formation of summary groups.

Platelet Rich Proteins preparation:

There are many ways to make PRP, and different centrifugal times, centrifugal force, and centrifugal time, PRP produced are different. In addition, the platelet recovery and activation rate in PRP can also be affected by factors such as different lengths of the axis, different diameters and lengths of the centrifuge tube, the material of the centrifuge tube (glass or plastic), and even different body positions or blood drawing at different times of the day.

PRP can be injected directly into the affected area or "activated" by adding calcium chloride or thrombin, which degranulates the activated platelets and releases growth factors and differentiation factors. After activation, about 70% of stored growth factors were released within 10min, and almost 100% were released within 1 h. The remaining few growth factors were released within 8–10 d of platelet survival. (5)

Role of PRP in osteoarthritis:

Osteoarthritis (OA) is a common and disabling condition associated with pain and the loss of mobility that undermines the quality of life. Clinically, the condition can be identified by many clinical symptoms, for example, joint pain, tenderness, stiffness, and limitation of movement with effusion and variable degrees of local inflammation. Pain in osteoarthritis is not simply attributable to the structural changes in the joint, but it is the result of coaction between structural change, and peripheral, and central pain processing mechanisms. (6) closure of the wound, hospitalizations, and infections.

Classification:

Over the past decade, PRP use has grown significantly with numerous formulations currently available. Several authors have attempted to classify these preparations to give the orthopedic community the means of comparing formulations, to find the optimal preparations for specific pathologies. This qualitative classification gave a starting point but did not take into consideration other subpopulations of cells such as RBCs or neutrophils, which have an important role in the mechanism of action of PRP. Magallon proposed a classification system focused on the quality of the preparation. The DEPA classification (Dose, Efficiency, Purity, Activation) analyses aspects of the production process that were not previously taken into consideration [8, 7].

Mechanism of action:

Platelets are anucleate cytoplasmic fragments of megakaryocytes that differentiate down the myeloid cell lineage. (9) They contain α-granules, often thought of as the storage units of platelets, which studies suggest containing an abundance of growth factors (GFs). Perhaps the biggest area of controversy surrounding PRP is the concentration of cellular components, particularly leucocytes. There has been debate around whether leucocytes are adverse

because of cytokines causing inflammation and subsequent weaker fibrotic tissue and/ or proteases and reactive oxygen species they release,50 or beneficial as a result of cytokines that can prevent infection and improve healing.16 This is something we will explore in the following section [12,11,10].

- Molecular mechanism of PRP:

PRP has seven basic proteins: PDGF, TGF-β, VEGF, EGF, hepatocyte growth factor (HGF), fibroblast growth factor (FGF), and IGF-1 (20). PDGF is a glycoprotein produced from platelet degranulation beside the injury. TGF-β is produced by platelets and macrophages and serves as an anti-proliferation factor in natural epithelial cells. Fibroblasts, marrow stem cells, andpre-osteoblasts are the target cells for TGF-β. [13] VEGF is a signaling protein secreted by cells and activates angiogenesis. EGF activates the growth, proliferation, and variation of the cells throughbinding to the receptor EGFR [14,15].

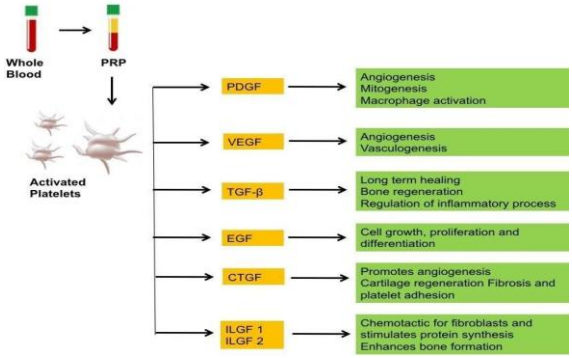

Figure 3: The main functions of platelet-rich plasma (PRP).

Clinical applications:

As a source of growth factors for many treatments, PRP has become an important clinical therapy. One of the greatest advantages of PRP is that it arrives to the injured area directly. PRP also helps regenerate damaged or worn tissue, the reducing back pain and increasing spinal function [16].

Infections of sternal wounds after heart surgery are common, and in some cases, can lead to death. PRP injections have been shown to improve the healing process and reduce the risk of infection. Excessive bleeding can sometimes occur during heart surgery. As a result, some patients need blood transfusions during surgery [17].

Limitations and prospects:

Although PRP has many theoretical functions and certain clinical application value, PRP is not used as a major treatment in practice. Currently, PRP is mainly used for cosmetic or dental treatment. At present, the controversy or disadvantage of PRP mainly lies in the two aspects of infection and abuse. [18]

Conclusion

PRP's simplicity, low cost, and minimally invasive nature have made it a popular therapy option for musculoskeletal problems. Regarding PRP's efficacy in treating tendinopathy and osteoarthritis, there are various disagreements in the literature itself.There should be more clinical research conducted to see whether PRP has any long-term benefits as interest in using it to treat musculoskeletal disorders grows. Currently, many studies only report short-term results, as is the case with many other injections. Every treatment we employ in clinical practice needs to be used with caution, but PRP and other injections especially so. It has been amply shown that people experience larger placebo effects from treatments such as platelet-rich plasma (PRP) because they believe it to be a more potent form of exercise and because they have a biological bias, therefore it should work. PDGF, TGF-β, VEGF, EGF, HGF, FGF, and IGF-1 are the seven fundamental proteins found in PRP. PRP has grown in importance as a therapeutic therapy since it provides growth factors for a variety of treatments.

There are significant gaps in the body of literature that currently exists. Small sample numbers, brief follow-up periods, and a lack of uniform protocols for PRP preparation are among the problems that make it difficult to compare the effectiveness of PRP across various research. The significant heterogeneity in PRP preparation combined with the variety in measured final outcomes and administration strategies, adds to the complexity.

Author contributions

All authors are contributed equally.

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Declaration of Competing Interest

The authors have no conflicts of interest to declare.

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